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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,209	09/28/2005	Denise M. Baker	2473.0260001/EKS/PAC	8322

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EXAMINER	
DIBRINO, MARIANNE NMN	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
04/26/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,209	BAKER ET AL.	
	Examiner	Art Unit	
	MARIANNE DIBRINO	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 January 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,16,23,26 and 31-40* is/are pending in the application.

4a) Of the above claim(s) *3-7,23,26,31, 33-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,16 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/19/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed 1/19/10 is acknowledged and has been entered.

2. Applicant is reminded of Applicant's election with traverse of species of (i) identifying from a particular antigen of a particular infectious agent variants of a class I MHC peptide epitope 8-11 amino acid residues in length, each variant comprising primary anchor residues of the same HLA class I binding motif, determining whether each of said variants comprises conserved, semi-conserved or non-conserved non-anchor residues in comparison to each of the remaining variants, and identifying a variant which comprises only conserved non-anchor residues in comparison to at least one remaining variant, in the response filed 6/11/09.

Claims 1, 2, 16 and 32 are currently being examined.

3. Applicant's amendment filed 1/19/10 has overcome the prior rejection of record of claims 16 and 32 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 1, 2, 16 and 32 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

A process claim, to be statutory under 35 U.S.C. 101, must pass the machine or transform test which ensures that the process in limited to a particular practical application, *i.e.*, in accordance with the M or T test, the claimed process must be (1) tied to a particular machine or apparatus, or (2) particularly transform a particular article to a different state or thing. The test ensures that the process is not simply claiming an abstract idea, mental process or substantially all practical uses of a law of nature or natural phenomenon.

In the instant case, the claims are drawn to a process that comprises purely mental steps.

Applicant may consider amending the claims to recite a method step wherein the candidate peptide epitope is tested for ability to induce a HLA class I CTL response against the variants of said peptide epitope.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:
A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

7. Claims 1, 2, 16 and 32 stand rejected under 35 U.S.C. 102(a) as being anticipated by De Groot *et al* (Immunology and Cell Biology, 2002, 80: 255-269, of record).

De Groot *et al* teach comparing the sequence of 8-11-mer peptides across strains of infectious agents such as HIV-1 to identify broadly conserved (cross-clade) epitopes (that contain motifs for binding a particular MHC class I molecule, that is, anchor residues, both primary and secondary), and further teach including in the method, the allowance of amino acid substitutions at non-anchor positions (see entire reference).

Although the reference does not explicitly teach that the non-anchor residues have only conservative substitutions, the reference does teach that the peptides have the anchor residues for binding a particular MHC class I molecule and that the peptides are conserved, *meaning that the amino acid residues at non-anchor positions are identical or conservative substitutions*. The art reference teaches that the degree of intra- and -interclade cross-reactivity will be determined by factors that include the degree of sequence conservation of CTL epitopes, *i.e.*, the degree of sequence conservation at all positions in the peptide, *meaning conservative substitutions*. The reference method teaches the step of looking for the most conserved potential epitope peptide sequences and additionally teaches that the step of allowing for amino acid substitutions for non-anchor residue positions may be performed while searching for the most conserved potential epitope peptide sequences. Thus, the reference method inherently teaches seeking conservative substitutions at the non-anchor positions as the most conserved sequences are chosen. In addition, the art reference method inherently teaches that the non-anchor positions are assessed for conserved, semi-conserved or non-conserved amino acid residues while doing this because knowledge of what is a conserved amino acid residue is necessarily also a comparison with what is not a conserved amino acid residue. Therefore, the claimed process appears to be the same or similar to the process of the prior art absent a showing of differences. Since the Patent Office does not have the facilities for examining and comparing the process of the instant invention to those of the prior art, the burden is on Applicant to show an unobvious distinction between the process of the instant invention and that of the prior art. See In re Best, 562 F2d 1252, 195 USPQ 430 (CCPA 1977).

Applicant's arguments have been fully considered but are not persuasive.

Applicant's said arguments are of record on pages 13-14 of the amendment filed 1/19/10.

However, with regard to said arguments, the transitional claim language is "comprising", meaning that other steps are encompassed by the claimed method such as comparing more than one potential epitope with its variants (*i.e.,* an 8-11-mer peptide subsequence of an antigenic protein), the art reference inherently teaches comparison of an epitope and its variants from one antigenic protein of an infectious agent, and Applicant is arguing a non-claimed limitation "using a single epitope as a starting point". For these reasons and those enunciated supra in the instant rejection, De Groot *et al* teach each and every element of the instant claims.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1, 2, 16 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over De Groot *et al* (Immunology and Cell Biology, 2002, 80: 255-269, of record) in view of Paul (Fund. Immunol. 5th Edition, Lippincott Williams & Wilkins, Philadelphia, pages 666-667, 2003).

De Groot *et al* teach comparing the sequence of 8-11-mer peptides across strains of infectious agents such as HIV-1 to identify broadly conserved (cross-clade) epitopes (that contain motifs for binding a particular MHC class I molecule, that is, anchor residues, both primary and secondary), and further teach including in the method, the allowance of amino acid substitutions at non-anchor positions. The art reference teaches that the degree of intra- and -interclade cross-reactivity will be determined by factors that include the degree of sequence conservation of CTL epitopes, *i.e.,* the degree of sequence conservation at all positions in the peptide.

De Groot *et al* do not *explicitly* teach that the non-anchor residues have only conservative substitutions.

Paul teaches that T cell receptors (TCRs) may distinguish different chemical classes of amino acid side chains. Paul teach that an example of structural differences between amino acid side chains recognized by the TCR comes from an analysis of non-cross reactive CTLs that distinguish homologous peptides from the V3 loop of different strains of HIV-1 envelope protein. Paul teaches that the two non-cross reactive TCRs recognize similar peptides but discriminate strongly between peptides with amino acids with aliphatic versus aromatic side chains, but on the other hand they do not distinguish strongly amongst different aliphatic residues or among different aromatic residues. Paul teaches that valine, leucine or isoleucine (conservative substituents) at a key TCR contact residue (position 8 of the peptide sequence) can be recognized by the same

TCR, while non-conservative substituent tyrosine can not and visa versa (paragraph spanning pages 666-667 and first full paragraph at column 1 on page 667).

However, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have selected for conservative substitutions at non-anchor residues.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this because those residues may serve as T cell contact residues, one of ordinary skill in the art was aware, as illustrated by Paul, that TCR have a degree of fine specificity but may be permissive of conservative substituents in the peptide, the primary art reference teaches that amino acid residues other than the primary anchor residues may also promote or interfere with binding to MHC and it also teaches that sequence conservation is important for peptide epitopes within and across HIV-1 clades that will react with CTLs .

Applicant's arguments have been fully considered but are not persuasive. Applicant's said arguments are of record on pages 13-14 of the amendment filed 1/19/10.

However, with regard to said arguments, the transitional claim language is "comprising", meaning that other steps are encompassed by the claimed method such as comparing more than one potential epitope with its variants (*i.e.,* an 8-11-mer peptide subsequence of an antigenic protein), the art reference inherently teaches comparison of an epitope and its variants from one antigenic protein of an infectious agent, and Applicant is arguing a non-claimed limitation "using a single epitope as a starting point".

Furthermore, with regard to Applicant's argument that the methodology disclosed in De Groot does not necessarily identify a candidate peptide epitope(s) that is able to induce a CTL response against variants of the peptide epitope, the instant claims recite "identifying a candidate peptide epitope"; likewise, De Groot *et al* clearly teach identifying candidate peptide epitopes, *i.e.,* they teach that the "algorithm has been used to map highly conserved T-cell [*i.e.,* CTL] epitopes in variable genomes (e.g., HIV-1 and HCV)" and that the methodology can "be used to identify broadly conserved (cross-clade) epitopes." (see especially second full paragraph on page 261).

With further regard to Applicant's argument that the Examiner has not provided a rationale for modifying the methodology of De Groot to arrive at the present invention, De Groot *et al* teach that it is desirable to identify broadly conserved epitopes, that HIV-1 is highly variant, that the algorithm for identifying the candidate peptide epitopes may be configured to allow substitutions at non-anchor positions, and that the most conserved peptide sequences from each HIV-1 protein of interest were chosen for study, all teachings that point to the obviousness of seeking conservative substitutions

at non-anchor positions (see especially page 261 starting at the second full paragraph, page 262 and page 263 at column 1, lines 1-8).

10. No claim is allowed.

11. With regard to reference "FP32" listed on page 1 of Applicant's Form 1449 filed 1/19/10, it is crossed-out because it is a duplicate citation.

12. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.
If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ram Shukla, can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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